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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,424	03/01/2002	Phillip Dan Cook	ISIS-5031	4700

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EXAMINER
BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
1639	9

DATE MAILED: 09/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/087,424	Cook
Examiner	**Art Unit**
Maurie G. Baker, Ph.D.	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *THREE* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 7, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *31-50* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *31-50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's Response filed July 7, 2003 (Paper No. 8) is acknowledged. No claims were cancelled or added and claims 34, 41 and 47 were amended. Claims 31-50 are pending and under examination.

Status of Rejections

2. The rejection under 35 U.S.C. 112, second paragraph is withdrawn in view of applicant's claim amendments. However, all other rejections are maintained. Applicant's arguments are addressed following each rejection.

Maintained Rejections
Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 31-50 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession of the invention. Applicant's claims are directed to a "method for preparing a library of compounds" comprising "contacting a purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms" with "at least six different chemical substituents". There are a virtually unlimited number of compounds that would fall within the claimed genus of "purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms" and "chemical substituents". The instant specification discloses only limited examples of carrying out the claimed method. This disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus.

Note that the language of the specification should describe the claimed invention so that one skilled in the art can recognize what is claimed. A description of a compound in terms of its function fails to distinguish the compound from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175).

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in University of California v. Eli Lilly and Co. (cited above) regarding disclosure. For adequate disclosure, like

enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co.* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure.

Response to Arguments

5. Applicant's arguments filed July 7, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

6. Applicant argues that the scope of the claimed genus of "purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms" and "chemical substituents" is not "virtually unlimited" as stated by the examiner. However, as there is no indication in the claim of the specific identity, location or attachment of the functionalizable atoms or the specific nature of the chemical substituents, the number of compounds that would fall within this scope would be extremely large (i.e. "virtually unlimited"). Note that in some claims, the chemical substituents can be attached via a tether moiety, which is another source of almost infinite variation.

7. The examiner's position is that the instant specification discloses only limited examples of carrying out the claimed method and that this disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Applicant argues that the instant specification adequately describes such entities and points to various portions thereof (Response, page 5, bottom). Although the specification does describe numerous examples, these examples are directed to a very limited set of molecules and represent only a very limited subset of the claimed genus of "purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms" and "chemical substituents" (attached either directly or via a tether moiety).

8. Note that a representative number of examples means that the species that are adequately described are representative of the entire genus. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. It is deemed that the instant specification lacks adequate support relating to the claimed genus and thus the above written description rejection is maintained.

Maintained Rejections
Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 31, 32, 34-36, 38, 39, 41-43 and 45-49 remain rejected under 35 U.S.C. 102(a) as being anticipated by Gordeev et al (WO 96/33972).

Gordeev et al disclose methods for synthesizing libraries of pyrimidine compounds (see Abstract). The library compounds of Gordeev et al have the claimed heterocyclic scaffold (see page 34-35 and more specifically page 81) and are substantially homogeneous (page 35, bottom). This reads specifically on instant claims 34, 41 and 47. The library compounds are made in a pooled format (see page 84, lines 18-28); for example, a pool of 21 pyrimidines is made and tested. This reads directly on the limitation of a mixture of at least 6 compounds and the further limitations of claims 35, 36, 42, 43, 48 and 49. All compounds are present in at least some of the pools and the compounds are synthesized at a purity (see page 81) where the mixture would be close to equimolarity (reading on claims 32, 39 and 46). The pyrimidine compounds of Gordeev et al have at least three functionalizable atoms, at least one of which is nitrogen and at least one of which is blocked (see pages 81-85 and Figure 10). In the compounds of Gordeev et al at least one substituent is attached via a tether; e.g. the tether can be considered to be the amine moiety (NHR^1). The building blocks of the library comprise various leaving groups (see page 83).

Response to Arguments

11. Applicant's arguments filed July 7, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

12. Applicant argues that instant claim 31 "*begins* with a purine or pyrimidine scaffold and appends substituents thereto" (Response, page 6). Applicant states that since the Gordeev et al reference "takes a mixture of amino acid precursors and reacts them to produce their respective guanidine derivatives", it does not anticipate the instant claims. The examiner respectfully disagrees.

13. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., beginning with a fully formed purine or pyrimidine scaffold and appending substituents thereto) are not recited in the rejected claim(s). There is no limitation in the instant claims that the purine or pyrimidine scaffold be fully formed before the contacting step. All that is necessary to meet the limitations of the claim is to contact a scaffold with a mixture of chemical substituents to form a "substituent-appended scaffold". Moreover, the claimed method is a method ***comprising***. See MPEP 2111.03: The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997). Thus, because the claims do not recite beginning with a fully formed scaffold and additional, unrecited method steps may be included, the examiner deems that the disclosure of the Gordeev et al reference reads on the instant claims.

14. For these reasons, the above rejection under 35 U.S.C. 102 is deemed to be proper and is maintained.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 31-50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Gordeev et al (WO 96/33972) in view of Smith et al (Bioorg. Med. Chem. Lett., 1994, Vol. 4, No. 24, pp. 2821-2824).

Gordeev et al teach methods for synthesizing libraries of pyrimidine compounds (see Abstract). The library compounds of Gordeev et al have the claimed heterocyclic scaffold (see page 34-35 and more specifically page 81) and are substantially homogeneous (page 35, bottom). This reads specifically on instant claims 34, 41 and 47. The library compounds are made in a pooled format (see page 84, lines 18-28); for example, a pool of 21 pyrimidines is made and tested. This reads directly on the limitation of a mixture of at least 6 compounds and the further limitations of claims 35, 36, 42, 43, 48 and 49. All compounds are present in at least some of the pools and the compounds are synthesized at a purity (see page 81) where the mixture would be close to equimolarity (reading on

claims 32, 39 and 46). The pyrimidine compounds of Gordeev et al have at least three functionalizable atoms, at least one of which is nitrogen and at least one of which is blocked (see pages 81-85 and Figure 10). In the compounds of Gordeev et al at least one substituent is attached via a tether; e.g. the tether can be considered to be the amine moiety (NHR^1). The building blocks of the library comprise various leaving groups (see page 83).

Gordeev et al lacks the teaching of carrying out the reaction in a single vessel and performing the reaction in solution phase.

However, it was well known in the art at the time of the invention to carry out combinatorial syntheses in a single vessel when using mixtures of reagents as well as carrying out reactions in solution phase. For example, Smith et al teaches the synthesis of chemical libraries in solution phase using a mixture of reactants (nucleophiles and acid chlorides), see page 2822 under *Library Synthesis*. The reactions were carried out each in a single vessel.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the method of Gordeev et al for synthesizing libraries of pyrimidine compounds utilizing the teachings of Smith et al for carrying out the reaction in a single vessel and performing the reaction in solution phase. A person of ordinary skill in the art would have been motivated to perform such a method because Smith et al teach that the use of mixtures can provide simplicity to the reactions and workup (see page 2822, top) and that the

formation of libraries in this format is useful for "rapid identification of chemical leads" (see Abstract).

Response to Arguments

17. Applicant's arguments filed July 7, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

18. Applicant argues that since the Gordeev et al reference does not anticipate claims 31, 32, 34-36, 38, 39, 41-43 and 45-49, the combination of the Gordeev et al and Smith et al references also does not render claims 31-50 obvious. The examiner maintains that the Gordeev et al reference anticipates the claims as discussed above (paragraphs 11-14) and thus also deems that the combination of the Gordeev et al and Smith et al references is proper. Thus, the above rejection under 35 U.S.C. 103(a) is also maintained.

Status of Claims/ Conclusion

19. No claims are allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the

advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

22. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
September 22, 2003

MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER